

# Animal Bites and Zoonosis



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# Disclosures



- ▮ Views are my own opinion, and not those of the US Army or WRAIR
- ▮ I have no financial relationships with any of the products / companies discussed



# Outline



- Dogs
- Cats
- Other pets
- Exotics
- Review

A few cases along the way...





## □ Bite Infections

- ! mix of anaerobes and aerobes from patient's skin and animal's oral cavity

## □ Zoonosis

- ! Animal disease that is transmissible to humans (humans are usually an accidental host)
- ! Spread by aerosols, feces, urine, insects, and direct skin contact



# Bites



- ▢ 1% of all ER visits
- ▢ 60% related to dogs, 10% -20% cats
- ▢ Dog bites account for \$1 Billion/year in USA
- ▢ Age and gender
  - ! Age <20 and males more frequent victims for all bites
  - ! Females and elderly more common in cat bites
- ▢ Exotic animals



# Dogs



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# Dogs



## **Risk of Bite injury**

- ▢ Type of dog
  - ⚠ Working dogs and aggressive breeds at higher risk
  - ⚠ Pit bull terrier, Rottweiler, German shepherd, Akita
- ▢ Age of victim
  - ⚠ Young boys (age 5 – 9)

## **Area of bite**

- ⚠ Children: face, head and neck
- ⚠ Adults: hand, face, scalp, neck, thigh, leg

## **Type of bite**

- ⚠ Severe crushing injury can cause depressed skull fracture, severe scalp and intracranial bleed, facial disfigurement, damage to the great vessels and nerves







# Dog Bites - organisms



## ▢ Aerobic

- ! ***Pasteurella canis.***
- ! *Streptococcus* spp.
- ! ***Staphylococcus* spp.**
- ! *Neisseria* spp.

## ▢ Anaerobic

- ! *Fusobacterium* spp.
- ! *Bacteroides* spp.
- ! *Porphyromonas* spp.
- ! *Prevotella* spp.
- ! ***Capnocytophaga canimorsus***



# Dog Bites



- ▮ Only 2 – 10% get infected-Augmentin is drug of choice (Zosyn IV)
- ▮ *Pasteurella spp.*
  - ❗ Resistant to: cephalexin, clinda, diclox, erythro
  - ❗ Susceptible to: PCNs/cephalosporins, FQs, Doxy, TMP/SMX
- ▮ *Capnocytophaga spp.* (very bad in asplenic patients)
  - ❗ Resist to: TMP/SMX, ? vancomycin
  - ❗ Susceptible to: Amox/Clav, PCN G, clindamycin
- ▮ *Staphylococcus aureus*
  - ❗ MSSA > MRSA



# Cat Bites



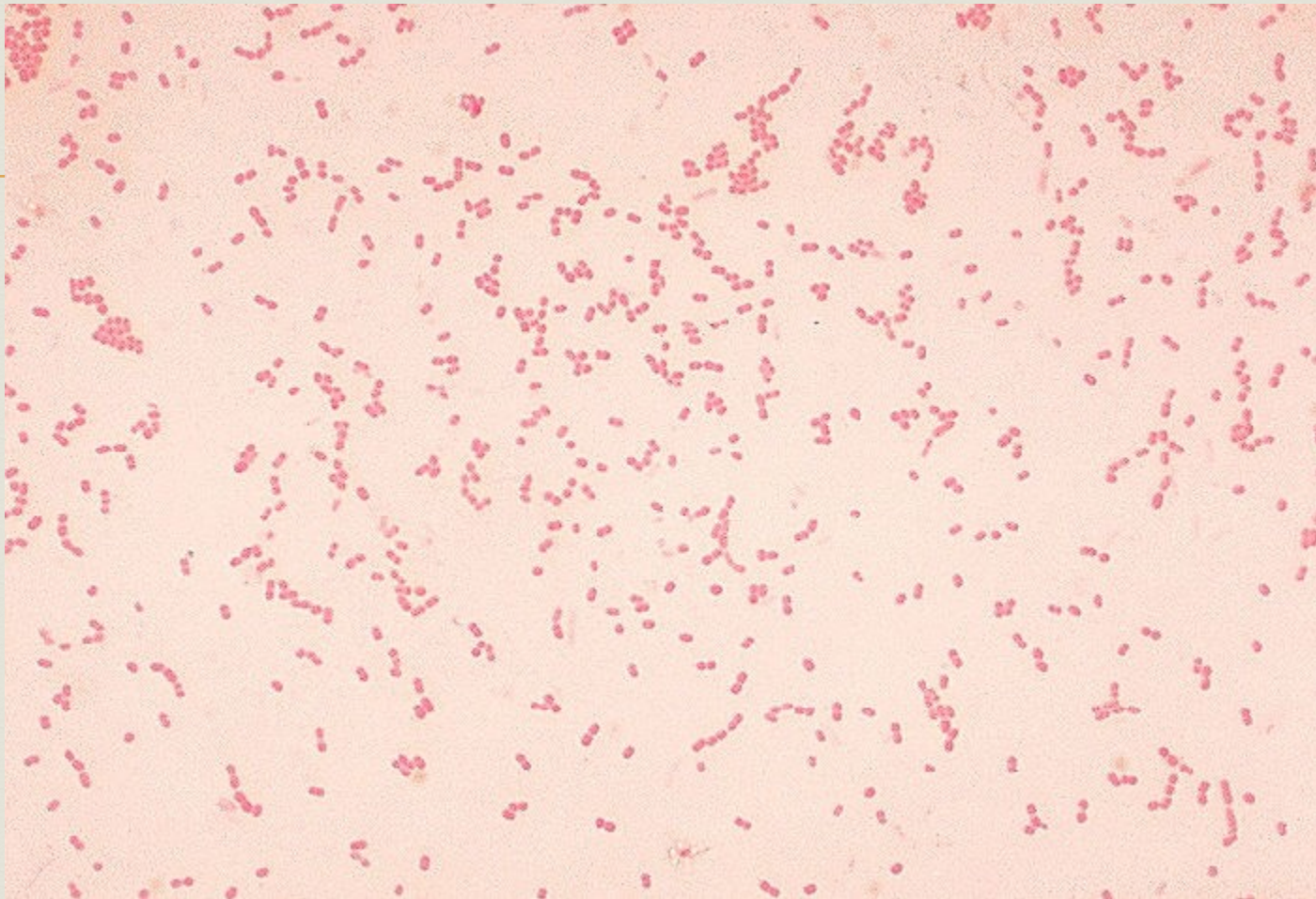


# *Pasteurella multocida*



- ▮ In saliva of >90% of cats, over 80% of wounds get infected
- ▮ Different species, *Pasteurella canis*, in saliva of 50% dogs, only 2 – 8% get infected
- ▮ Small aerobic GN bacilli
- ▮ Amoxicillin-sensitive





fastidious gram-negative bacillus



# *Pasteurella multocida*



- ▢ Cause serious infections
  - ✱ Necrotizing fasciitis
  - ✱ Septic arthritis
  - ✱ Osteomyelitis
  - ✱ Less commonly, sepsis, septic shock, pneumonia, and meningitis
- ▢ High risk groups for severe infection:
  - ✱ Infants
  - ✱ Pregnant women
  - ✱ Patients with evidence of notable liver disease
  - ✱ Patients on chronic steroids
  - ✱ HIV-positive individuals
  - ✱ Organ-transplant recipients
  - ✱ Other immunocompromised patients
- ▢ Mortality with severe infection remains substantial at 25%



# Cats



**Septic arthritis of left first proximal  
interphalangeal joint**

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# Girl vs Cat



- ❑ 15 y/o female with wound from cat on forearm
- ❑ Seen in ED, wound cleaned, treated with amox/clav orally
- ❑ Wound slowly became worse, somewhat ulcerative. Patient now back in ED for further evaluation.
- ❑ Upon further questioning, she had a history of recurrent infections





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**infection of the left forearm of a 15-year-old**



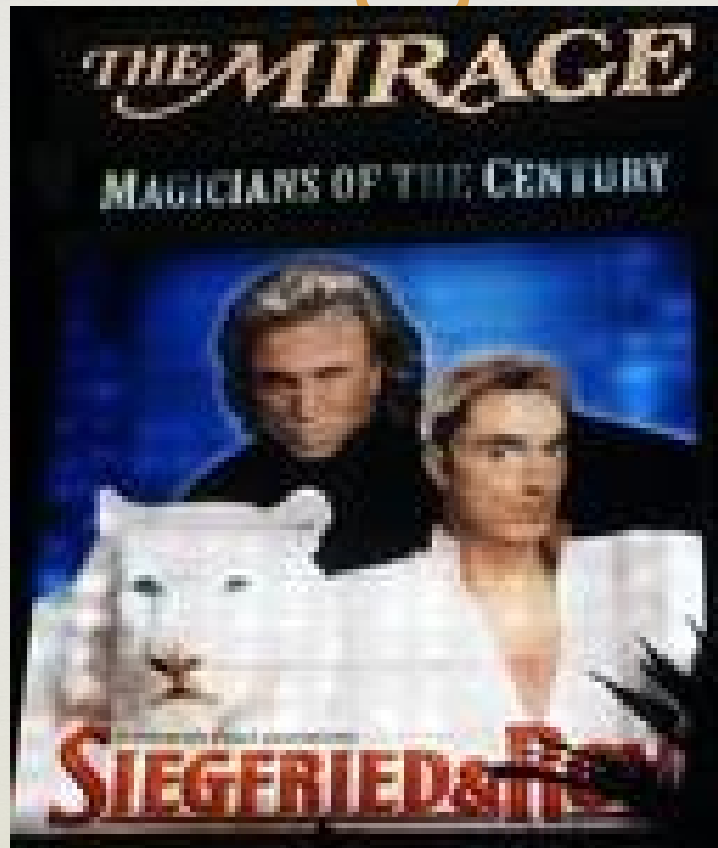


**Cat had developed recurrent MRSA culture  
positive skin  
lesions of the perineal area**

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# Roy Horn of Siegfried and Roy attacked by tiger



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# Don't try this at home...or abroad





# Tiger Bite



- ▮ September 18, 2003, a group of U.S. Army Reserve soldiers and Iraqi police were patrolling in the zoo after it had closed.
- ▮ A soldier had his right arm severely mauled by a male Bengal tiger; he had reportedly attempted to feed the tiger a chicken kabob
- ▮ Bystanders, seeing the attack, shot and killed the animal
- ▮ Bleeding was stopped, wound debrided, placed on broad spectrum ABX and patient medevac'd to WRAMC for further debridement and therapy



# *Acinetobacter baumanii*

- Environmentally present
- Occurs in many of the wounded coming in from theater
- Treated with further wound revision, broad spectrum ABX to include Amox/Sulbact and colistin, wound eventually healed
- Sustained a substantial amputation of arm in sequential surgical revisions



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*"We'll have to clean that out immediately...  
there's nothing dirtier than a lawyer bite."*



# Human Bites



- ❑ 52 y/o male suffers a hand injury in brawl at tailgate party in Baltimore
- ❑ Presents 12 hrs later with a swollen, red, painful fist. X-ray shows bony fragments. Wound cleaned and given cephalexin, ice, rest.
- ❑ Returns to ER 5 days later with tachycardia, hypotension, fever, confusion
- ❑ Small wound with minimal serous secretions on the dorsum proximal 3<sup>rd</sup> phalanx of left hand; warmth, edema, painful movement of phalanx, decreased sensation, no crepitation detected









- As soon as clinical evaluation was finished, anti-tetanic immunization was performed, and patient transferred to surgery room
- Pressure in dorsal compartment was (20mm Hg) and in palmar compartment (42 mm Hg)
- Purulent material (about 120 ml) drained from pre-retinacular space
- 1 g amox-sulbact IV q 6 hours





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# *Eikenella corrodens*



- ▢ Anaerobic small GN bacilli
- ▢ Common in human oral flora
- ▢ Resistant to:
  - ❗ cephalexin, clindamycin, erythromycin, Flagyl
- ▢ Susceptible to:
  - ❗ PCN, FQs, TMP/SMX, Doxy, ESC





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# Clinically significant Viral Zoonotic diseases



## Pathogen

Borna disease virus  
California serogroup viruses

Chikungunya virus

Cowpox virus  
Crimean–Congo  
haemorrhagic fever virus

Ebolavirus

Hantaviruses

Hendra virus

Hepatitis E virus

Influenza viruses

Japanese encephalitis virus

Kyasanur forest disease virus  
Lassa virus

Lymphocytic  
choriomeningitis virus  
Marburg virus

Monkeypox virus  
Nipah virus

Omsk haemorrhagic fever virus  
Oropouche virus  
Rabies and lyssaviruses

Rift Valley fever virus

Ross River virus

SARS coronavirus  
Sindbis virus  
Tick-borne encephalitis

Venezuelan equine  
encephalitis virus  
West Nile virus (WNV)

Yellow fever virus

Zika virus



# Clinically significant Bacterial Zoonotic Infections

## Pathogen

*Anaplasma phagocytophilum*

*Bacillus anthracis*  
*Bartonella* sp.

*Borrelia* sp.

*Brucella* sp.

*Burkholderia mallei* and  
*Burkholderia pseudomallei*  
*Campylobacter* sp.

*Capnocytophaga canimorsus* and  
*Capnocytophaga cynodegmi*  
*Chlamydia psittaci*

*Clostridium* sp.

*Corynebacterium ulcerans*

*Coxiella burnetii*

*Ehrlichia chaffeensis* and  
*Ehrlichia ewingi*  
*Escherichia coli*

*Francisella tularensis*

*Helicobacter* sp.

*Leptospira* sp.

*Listeria* sp.

*Mycobacterium* sp.

*Orientia tsutsugamushi*

*Pasteurella* sp.

*Rickettsia* sp.

*Salmonella* sp.

*Shigella* sp.

*Staphylococcus aureus*

*Streptococcus* sp.

*Vibrio* sp.

*Yersinia* sp.



# Horses

- Fecal transmission unlikely, but considered in those with close equine contacts
  - ❗ Salmonella
    - Usually mild, self limited disease
    - Severe cases (septicemia, meningitis) in immunocompromised
  - ❗ Campylobacter
    - Incubation 1 – 7 days
    - Abdominal pain and bloody diarrhea
  - ❗ Cryptosporidium
    - Rarely from healthy horses
    - Intracellular protozoan parasite
    - *C. parvum* and *C. hominis* are the likely human pathogens
  - ❗ *Giardia lamblia*-
    - directly or thru contaminated water
  - ❗ *Clostridium difficile*-
    - no horse-to-man transmission



# Horses



## □ Aerosol

### ! *Rhodococcus equi*

- GP pleomorphic coccoid
- Found in the soil contaminated with herbivore manure
- Horses have lung disease, UC and mesenteric adenitis
- Humans – pulmonary infection most common occurs in immunocompromised

## □ Pathogens also found in sheep and cattle:

### ! *Brucella suis* and *abortus*

- exposure to blood and body Fluids

### ! *Coxiella burnetti*

- Q fever
- Generally flu-like illness, pneumonia, hepatitis
- Chronic infection results in endocarditis



# Horses



- Mosquito-borne disease
  - ! EEE, WEE, West Nile virus: low/undetectable viremia; no reservoir for further spread
  - ! VEE: horse is primary amplification host
    - Prevent by immunizing horses
    - Found in FLA to South America
    - Incubate 1-6 days in man
    - 0.5% adults on 4% children develop encephalitis
- Infected saliva
  - ! Rabies unlikely but possible



# Rabbits?



- ▮ 22 y/o male acute fever, lymphadenopathy, malaise, and dry, non-productive cough in Martha's Vineyard
- ▮ 5 pack-year smoker, mows lawns at the Golf club. No reports of running over any animals nor handling animal carcasses
- ▮ CXR showed RLL pneumonia, with some findings on LLL (Bilat?)

Engl J Med 2001; 345:1601-1606 [November 29, 2001](#)

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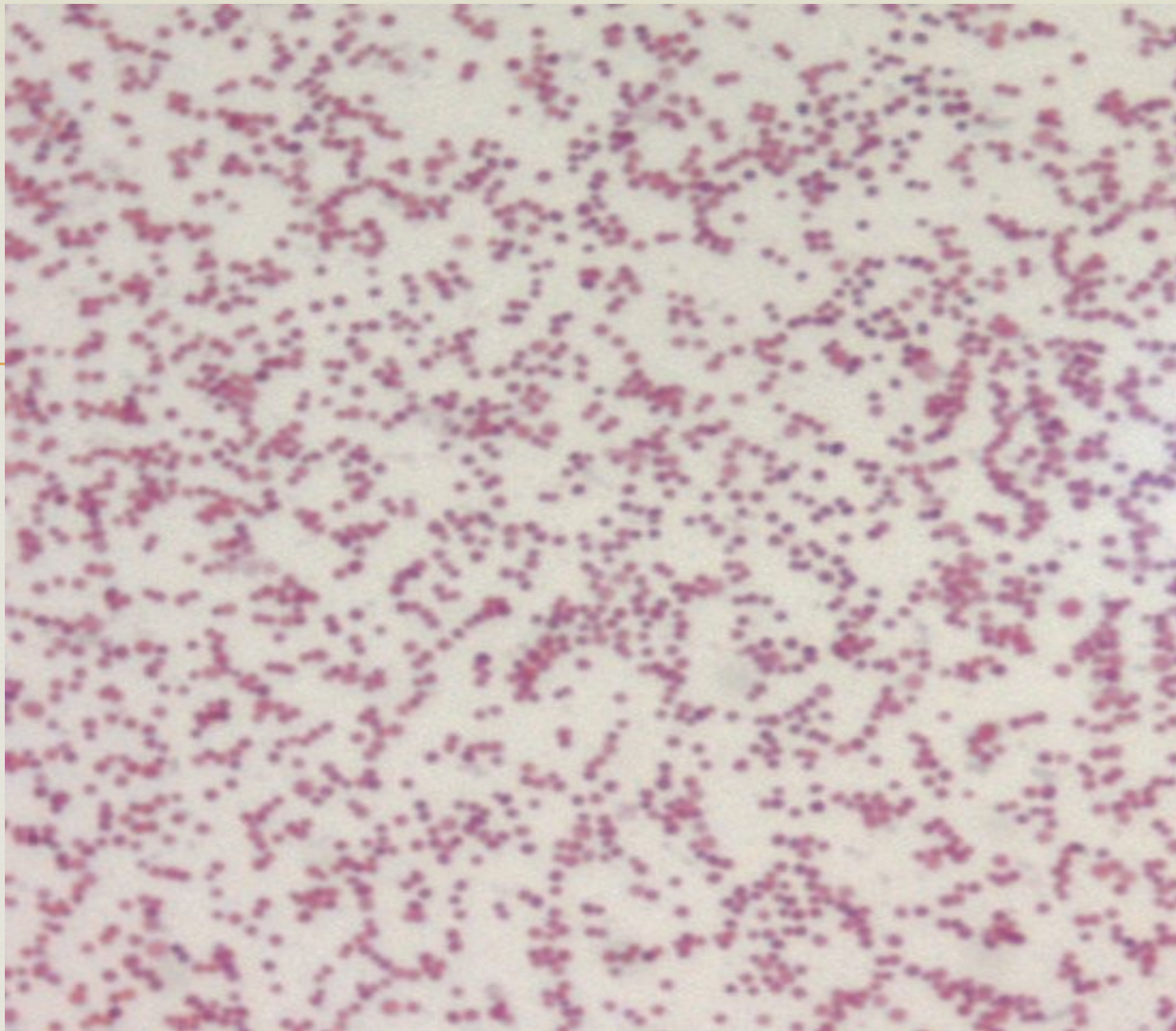


# Differential



- ▮ Typhoidal syndromes such as salmonellosis or rickettsial infections should be included in the differential diagnosis.
- ▮ Other causes of pneumonia such as infection with *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Coxiella burnetii*, or *Chlamydia psittaci*, as well as exposure to *staphylococcal* enterotoxin B
- ▮ In fulminant pneumonias, plague and inhalational anthrax





Tiny, pleomorphic, poorly staining gram-negative coccobacillus (0.2 to 0.5 by 0.7 to 1.0 microns). In clinical specimens, these forms can be found intracellularly.



# Rabbits

## □ GI

- ! ~~*Salmonella*, *Yersinia pseudotuberculosis*, *cryptococcus* spp.~~

## □ Respiratory

- ! *Pasteurella multocida* (no bunny-to-man trans) causes eye infections and snuffles in rabbits
- ! *Bordetella bronchiseptica* respiratory infection that can transmit to man

## □ Neurologic

- ! Rabies reported in 7 rabbits (chance encounter, generally doesn't happen)

## □ Cutaneous

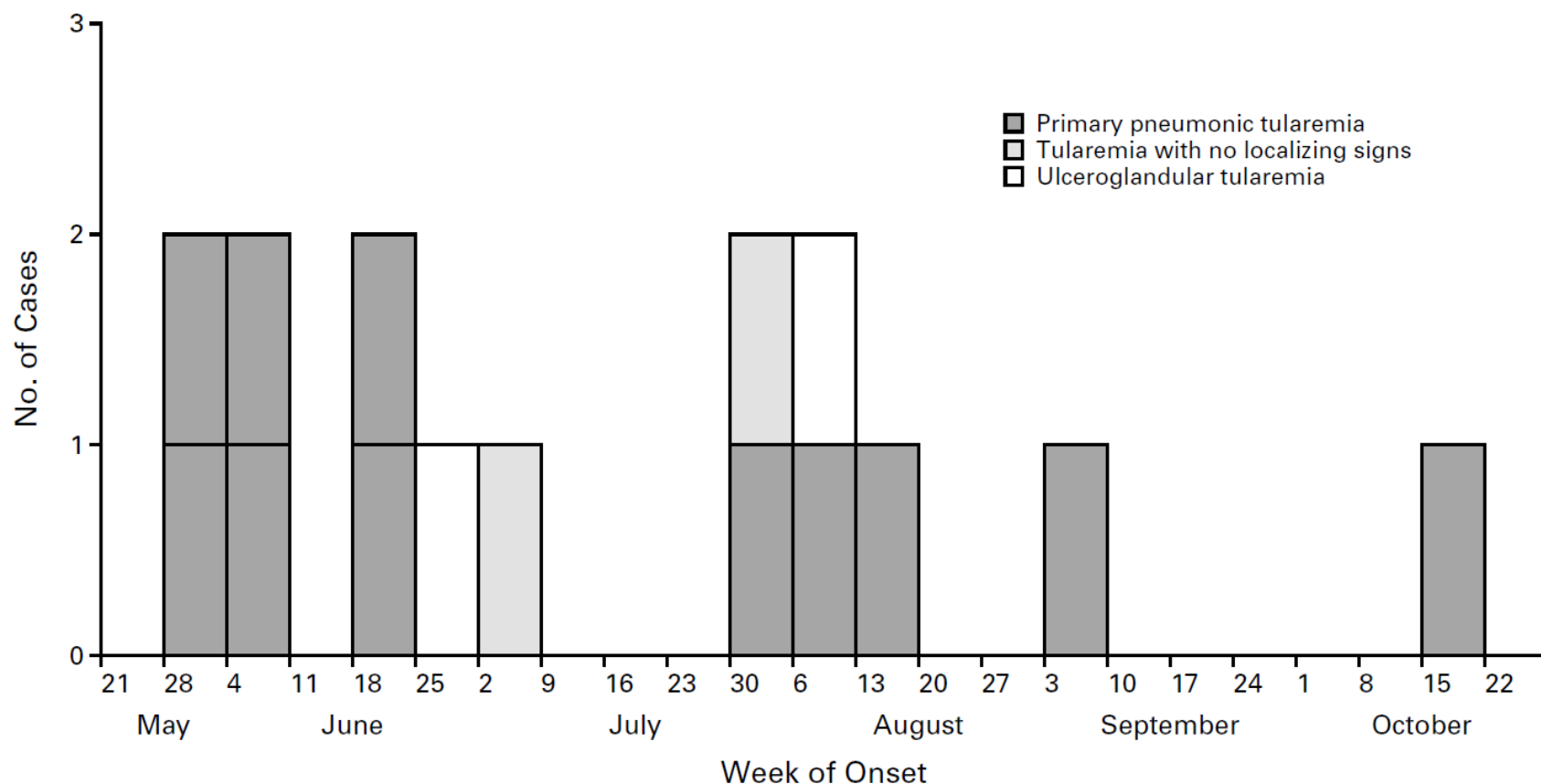
- ! Dermatophytes (ringworm) transmitted by direct skin contact

## □ Zoonoses

- ! Tularemia
- ! Babesiosis



## AN OUTBREAK OF PRIMARY PNEUMONIC TULAREMIA ON MARTHA'S VINEYARD



**Figure 1.** Cases of Primary Pneumonic Tularemia, Tularemia with No Localizing Signs, and Ulceroglandular Tularemia on Martha's Vineyard, May 21 through October 28, 2000, According to the Week of Onset of Illness.



# Tularemia



- Although *F. tularensis* does not form spores, it can survive in water, soil, and decaying animal carcasses
- The organism persists in water and mud for as long as 14 weeks, in straw for 6 months, and in oats for 4 months
- *F. tularensis* was shed in animal excreta, persisted in the environment, and infected people after being mechanically aerosolized and inhaled



# Tularemia: 6 Presentations



## □ *Typhoidal*

- ❗ Bacteremia with fever, chills, headache, myalgias, malaise, sore throat, and anorexia.
- ❗ Abdominal pain, nausea, vomiting, and diarrhea may be present

## □ *Pneumonic*

- ❗ Dry, non-productive cough, dyspnea, pleuritic chest pain, and fever.
- ❗ Physical examination may reveal rales, consolidation, and a friction rub or signs of effusion

## □ *Oculoglandular*

- ❗ painful, often purulent, conjunctivitis with lymphadenopathy especially in the periauricular, submandibular, and cervical areas



# Tularemia: 6

## Presentations (cont'd)

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### □ *Oropharyngeal*

- ❗ painful sore throat; there may also be abdominal pain, nausea and vomiting

### □ *Ulceroglandular*

- ❗ Regional lymphadenopathy with a papule that develops into an ulcer at the site of entry. Fever, chills, headache, malaise, anorexia, and fatigue usually are the first symptoms

### □ *Glandular*

- ❗ similar to the ulceroglandular form, but without skin or mucous membrane lesions



# Diagnosis



- *F. tularensis* is difficult to culture on standard media
  - ❗ Send early post-exposure (<24 hrs) nasal swabs, sputum, induced respiratory secretions for culture, DFA
- Definitive diagnosis is usually made retrospectively by serology
  - ❗ Titers are usually negative during the first week



# Tularemia



## ▮ **Treatment:**

- ! Streptomycin 30 mg/kg qd IM for 10-14 days, or gentamicin 3-5 mg/kg qd IV for 10-14 days.

## ▮ **Prophylaxis:**

- ! A live, attenuated vaccine (available as an IND) is administered once by scarification
- ! Doxycycline 100 mg q12h po for 14 days, or
- ! Tetracycline 500 mg qid po for 14 days.



# Rodents



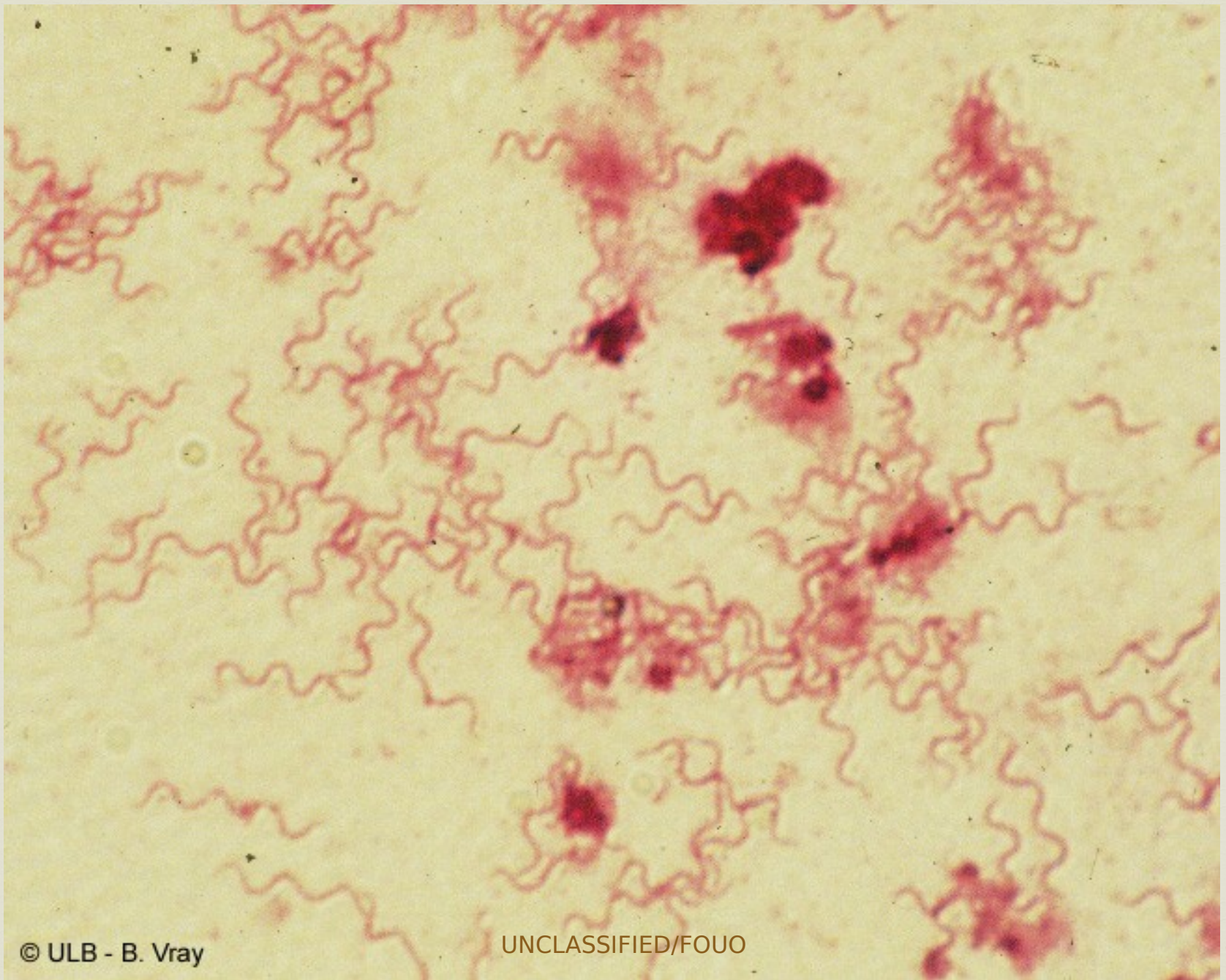
- ▢ Infected saliva
  - ! Tularemia
  - ! Rat bite fever
  - ! Rabies (VERY rare): 2005 case report of rabies in guinea pig in NY
- ▢ Direct contact or aerosol
  - ! LCMV (lymphocytic choriomeningitis virus)
    - ▢ Transmission to man thru direct contact with fomites or aerosolization of virus
  - ! Monkeypox
    - ▢ Prairie dogs in the flea market
  - ! Cowpox
  - ! Ringworm
  - ! Hantavirus



# Clubbing with the rat pack

- ▣ 48 y/o male in SE Asia comes to the clinic with fevers and severe myalgias
- ▣ He had been slipped a ruffi while at a club, bushwacked when exiting, roughed up, robbed and left in a back alley, awakening in his own filth, shoes, valuables and ID all stolen
- ▣ No evidence of sexual assault
- ▣ On PE, animal bite marks around right ankle
- ▣ Faint rash on extremities
- ▣ Within 24hrs, blood cultures positive for pleomorphic GNR







# Rat Bite fever



- ▢ *Spirillum minus* in Asia
- ▢ *Streptobacillus moniliformis* in USA
- ▢ Children, poor, pet shops, labs
- ▢ Symptoms:
  - ❗ Fever
  - ❗ Rash (mac/pap, pustular, petechial, purpuric)
  - ❗ Polyarthralgias
  - ❗ Haverhill Fever (unpasteurized milk outbreak)
- ▢ Treatment:
  - ❗ PCN, Doxy



# Birds



- ▢ Pet birds
- ▢ *Chlamydophila psittaci*:
  - ! found in almost all pet birds, shed in feces and nasal discharge
  - ! 1988-2003, 935 human cases in USA
- ▢ *Cryptococcus neoformans*
  - ! Found in soil, from bird feces
  - ! Inhalation of basidiospores or poorly encapsulated yeast
  - ! Generally in the immunocompromised
- ▢ Wild birds
  - ! Avian influenza
  - ! West Nile virus





## ▢ Psittacosis

- ! Fever, HA and dry cough with recent bird exposure
- ! Pharyngitis, diarrhea and rarely encephalitis
- ! DX by serology, DFA, PCR
- ! Do NOT culture: grade 3 pathogen
- ! Tx with tetracycline; erythromycin (alternative)

## ▢ Cryptococcus

- ! Cough, chest pain, fever, wt loss, hemoptysis
- ! Uncommon: dyspnea, rash night sweats
- ! DX by histo, fungal cult, serum crypto Ag, x-ray
- ! Tx: fluconazole, itra, posi, vori in immunocompetent pt





## □ Ferrets

- ! Influenza: aerosols from infected ferrets
- ! Giardia, Salmonella, Campylobacter, Cryptosporidium
- ! *Mycobacterium microte* (vole TB)
- ! No rabies transmission documented (vaccinate!)

## □ Hedgehogs

- ! Salmonella, Yersinia, dermatophytes (Trichophyton)

## □ Flying squirrels

- ! Toxo, Staph, *R. prowazeckii* (epidemic typhus)

## □ Chinchillas

- ! Dermatophytes
- ! Klebsiella and Pseudomonas (no known transmission)



# Slow growing ulcer in a Sudanese 10 year- old





# Buruli Ulcer



- ▢ *Mycobacterium ulcerans*
- ▢ 3<sup>rd</sup> most common mycobacterial disease in humans
- ▢ Present in West Africa, East Africa, Papua New Guinea, Indonesia
- ▢ Carried by various animals and insects, including opossums, koalas, African clawed frogs, amadillos, water bugs



# Fish



- Water exposures:
  - ! *Mycobacterium marinum*
  - ! Additional occupational exposures:
    - *Aeromonas hydrophilia*
    - *Edwardsiella tarda*
    - *Erysipelothrix rhusiopathiae*
- Shellfish insult
- Parasites



# Tanks a lot...

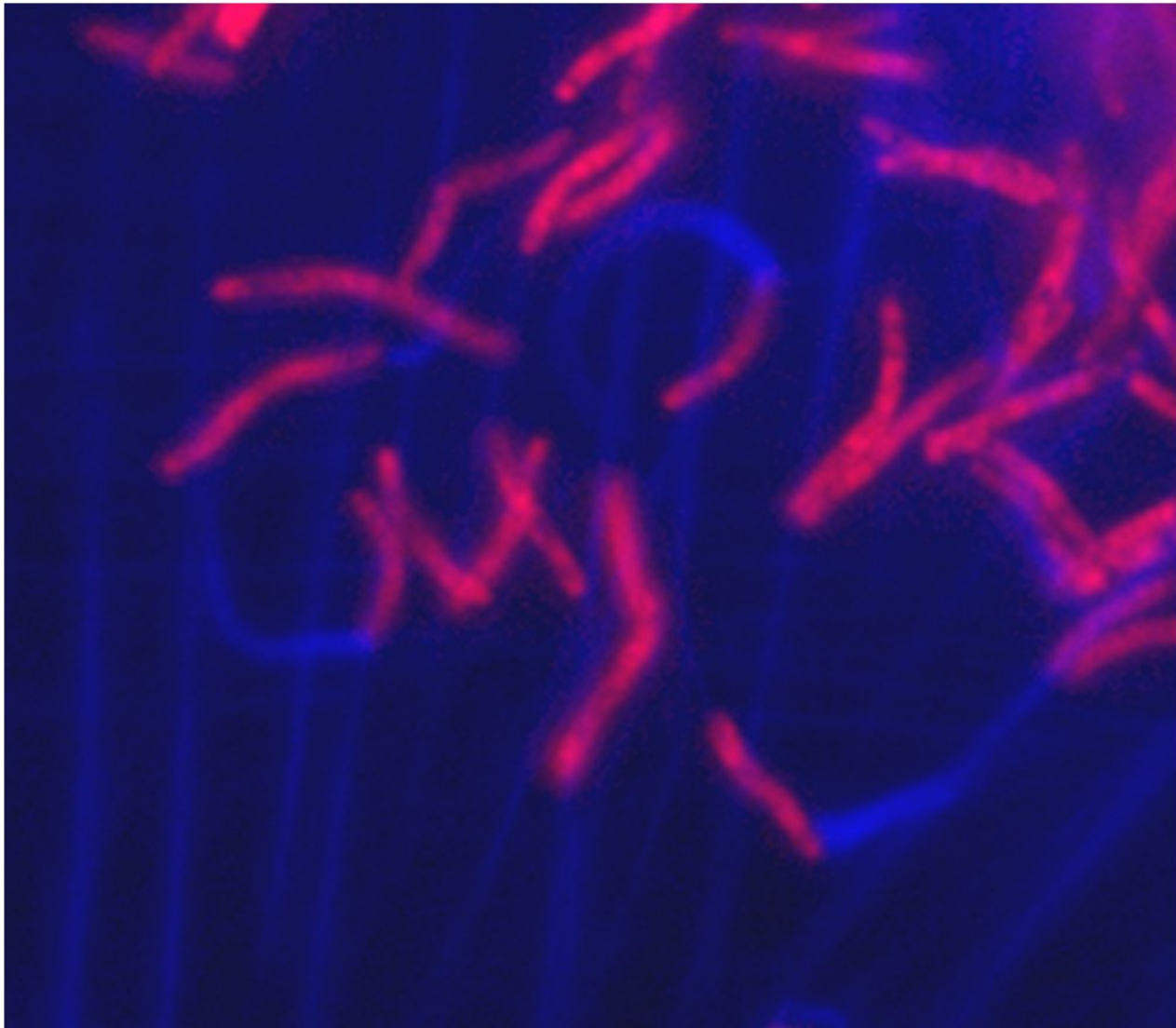


- ▮ 22 year old grad student had after-work job at pet shop (fired 3 weeks ago)
- ▮ Sustained minor abrasion on underside of tank/plastic branch, while cleaning aquarium
- ▮ Now with lesion on dorsum of hand, not healing, not responsive to topical antibiotic ointment and cephalexin









Acid fast stain  
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# *Mycobacterium marinum*

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- ▢ Found in fresh and salt water (swimming pools, fish tanks)
- ▢ “Fish tank granuloma” caused while sustaining minor injury or abrasion while cleaning fish tank
- ▢ Cutaneous lesions: soft skin papules, pustules and ulcers developing weeks after an injury/exposure
- ▢ Treatment options: rifampin plus ethambutol, tetracyclines, TMP-SMX , clarithromycin and fluoroquinolones



# fishy case of shellfish?

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- ▮ 53 y/o gulf bay fisherman, alcoholic with cirrhosis, has abrasions on arm/leg while harvesting oysters
- ▮ Few hours later, red, painful skin, hemorrhagic bullae begin to develop on legs and hands/arms
- ▮ Comes into the clinic not well 36 hrs later, in pain





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# *Vibrio vulnificus*



- ▮ Leading cause of shellfish associated deaths in USA
- ▮ Wound exposure to salt/brackish water in warm summer months
- ▮ Filter-feeding shellfish (i.e. oysters) concentrate bacteria
- ▮ Risk factors for severe disease:
  - ❗ Liver disease, hemochromatosis, alcohol abuse
- ▮ Treatment : doxy + ceftriaxone (or FQ)



# *Vibrio vulnificus*



## **Preventive measures**

- ❑ Avoid exposing open wounds to warm seawater; cover with water-tight wrap.
- ❑ Wear gloves when handling raw shellfish and avoid cross-contamination of raw shellfish with other foods
- ❑ Cook shellfish thoroughly; if considered high risk, do not consume raw oysters or other shellfish



# Fear the Turtle





# Reptiles



- ▮ 74-90% colonized with Salmonella
- ▮ Intermittently shed in feces
- ▮ Responsible for 6% (74,000 cases) of salmonella cases in US
- ▮ Yersinia, Campylobacter, Aeromonas
- ▮ Sale of turtles with carapace < 4 banned in 1975 resulted in decrease of Salmonella cases in children by 100k





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# Monkeys



- ▮ Few reports of disease transmission from pet monkeys
- ▮ Shigella and Salmonella have been transmitted from asymptomatic spider monkeys
- ▮ Herpes B
  - ❗ Cercopethicine herpes virus 1
  - ❗ Transmitted directly from rhesus macaques through bites or scratches or from tissues or fluids
  - ❗ 80 – 90% of adult macaques infected and usually asymptomatic



# B virus



- ❑ In monkeys, either no lesions or oral/genital lesions (HSV for monkeys)
- ❑ Viral shed is lifelong in oral and genital secretions, conjunctiva
- ❑ In humans, leads to encephalitis, fatal in 80% without treatment
- ❑ Majority of cases are in those who work with non-human primates



# B Virus – Who is at risk?

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- Monkey handlers
- Travelers exposure to free-ranging monkeys
  - ! India, Indonesia and Nepal
  - ! Puerto Rico and the Caribbean
- Those with monkeys kept as pets




# B Virus – clinical manifestations

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- 1
  - ❗ Vesicular or ulcerative lesions
  - ❗ Tingling, pain or itching at site
  - ❗ Local lymphadenopathy
- 2
  - ❗ Influenza like illness (fever and myalgias)
  - ❗ Numbness, paresthesias, fever, conjunctivitis, abdominal pain, hepatitis, pneumonitis, CNS symptoms
- 3
  - ❗ Nausea and vomiting
  - ❗ CNS symptoms including HA, CN deficits, dysarthria, dysphagia, seizures, paralysis, respiratory failure and coma



# B Virus: Post exposure Indications

- 
- ▢ Skin or mucosal exposures to animals that are at high risk of shedding B virus
    - ❗ ill or immunocompromised macaques, animals with oral or genital lesions, or animals known to be shedding virus)
  - ▢ Inadequately cleaned skin or mucosal exposures
  - ▢ Lacerations of the head, neck, or torso
  - ▢ Deep puncture bites
  - ▢ Needlestick injuries with possibly contaminated needle
  - ▢ Lacerations or puncture wounds with contaminated objects
  - ▢ Exposures in which post-cleansing cultures are positive for B virus



# B Virus: Post exposure



- Wash wound for 15 minutes
  - ❗ Skin: chlorhexidine, detergent or bleach (1:20)
  - ❗ Eyes, mucous membranes: flush with water
- Post-wash cultures of wound
- Treatment / prophylaxis
  - ❗ Acyclovir 800 mg po qid x2 weeks (PREGNANCY)
  - ❗ Valacyclovir 1g po tid x2 weeks (preferred for all others)
  - ❗ Suppressive treatment lifelong : valacyclovir 500 qd or acyclovir 400 tid
- Treatment/disease
  - ❗ If no CNS or PNS findings: IV Acyclovir
  - ❗ If CNS or PNS findings: IV Gancyclovir



# Rabies



- ▮ Highest case-fatality rate of any known infectious disease (>99% Fatal)



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# The Military Relevant Story ...

## A 40 yr old Master Sergeant

### Near Balad Iraq:

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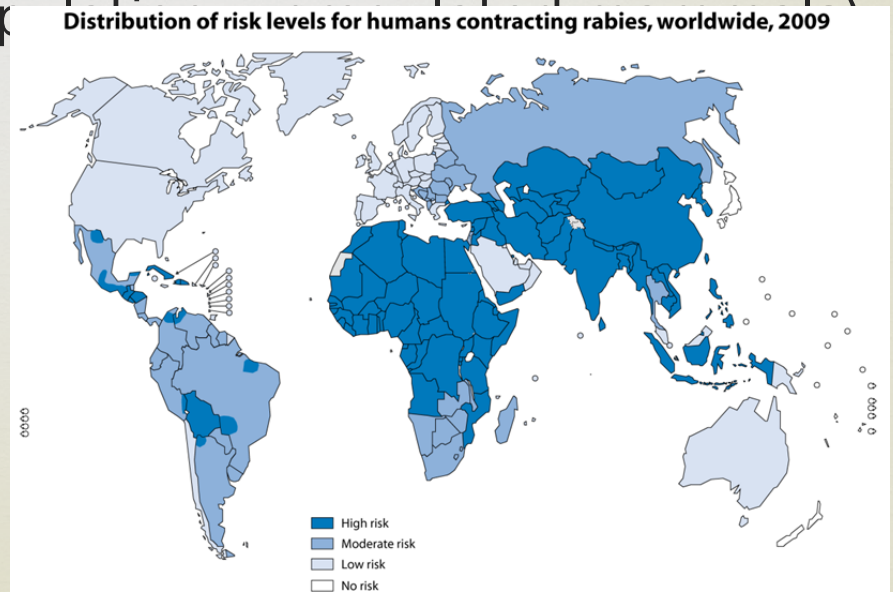
- ❑ Out in FOB with other NCO's
- ❑ "Unknown" small cat appears tangled in the camouflage netting
- ❑ He tries to free up this feral cat
- ❑ Cat bites his palm, then runs off
- ❑ No one can identify cat's location, after an extensive search...





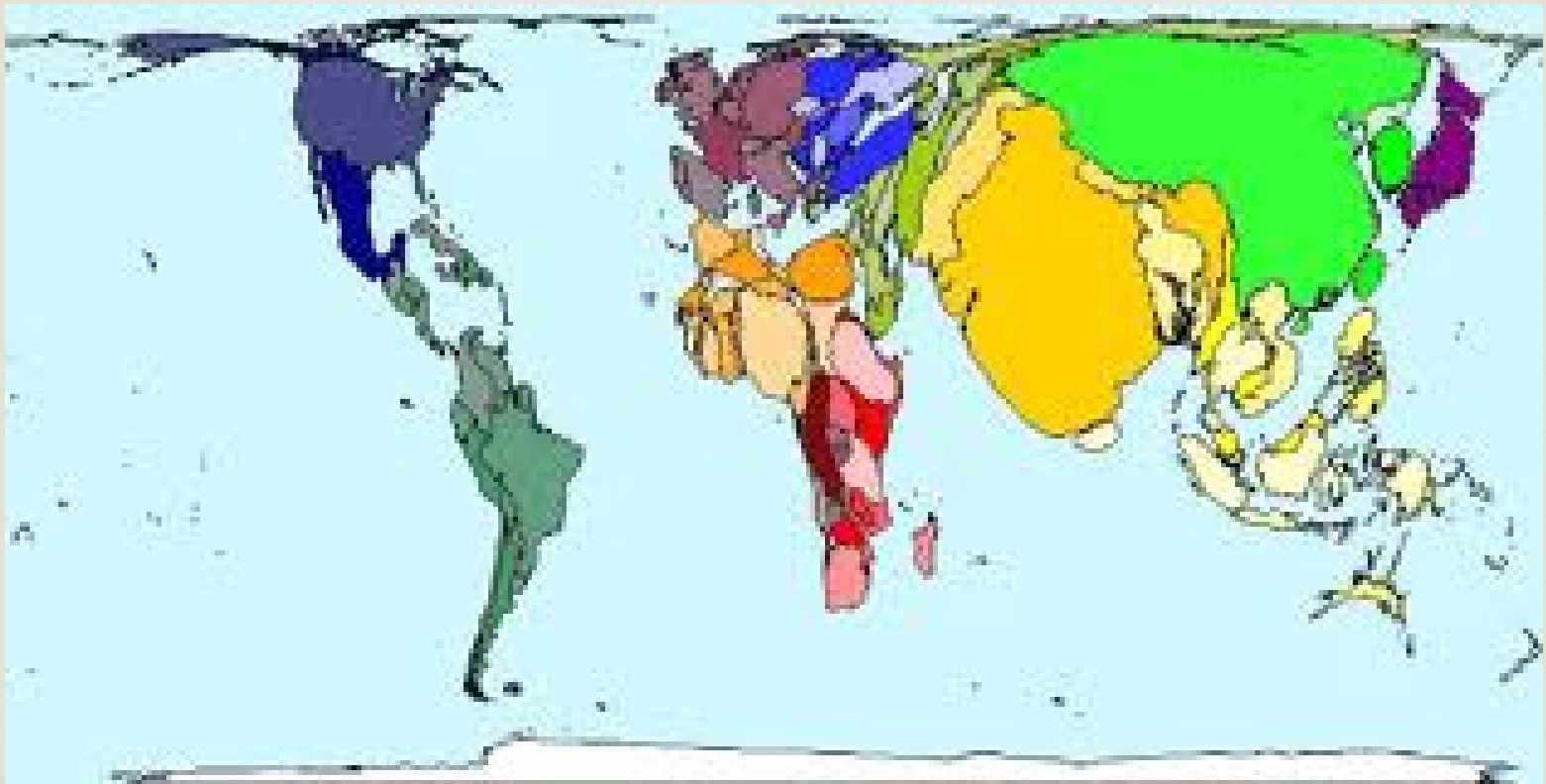
# Varied Practices/Environments - Result in Distinctly Regional Epidemiology

- ▢ Probably most rabies may have originated in **bats**
- ▢ But, most human spillover occurs from intermediate mammalian reservoirs
- ▢ **Worldwide ~40 - 60K human cases *reported*** to WHO annually
- ▢ Majority of cases are in the developing world –
  - ⚠ India >30,000 cases/year (Pop
  - ⚠ Often undiagnosed
- ▢ 10 million human PEP's yearly
  - ⚠ 5 million in China
  - ⚠ 1 million in India
  - ⚠ 40-60,000 in N. America





# Cases

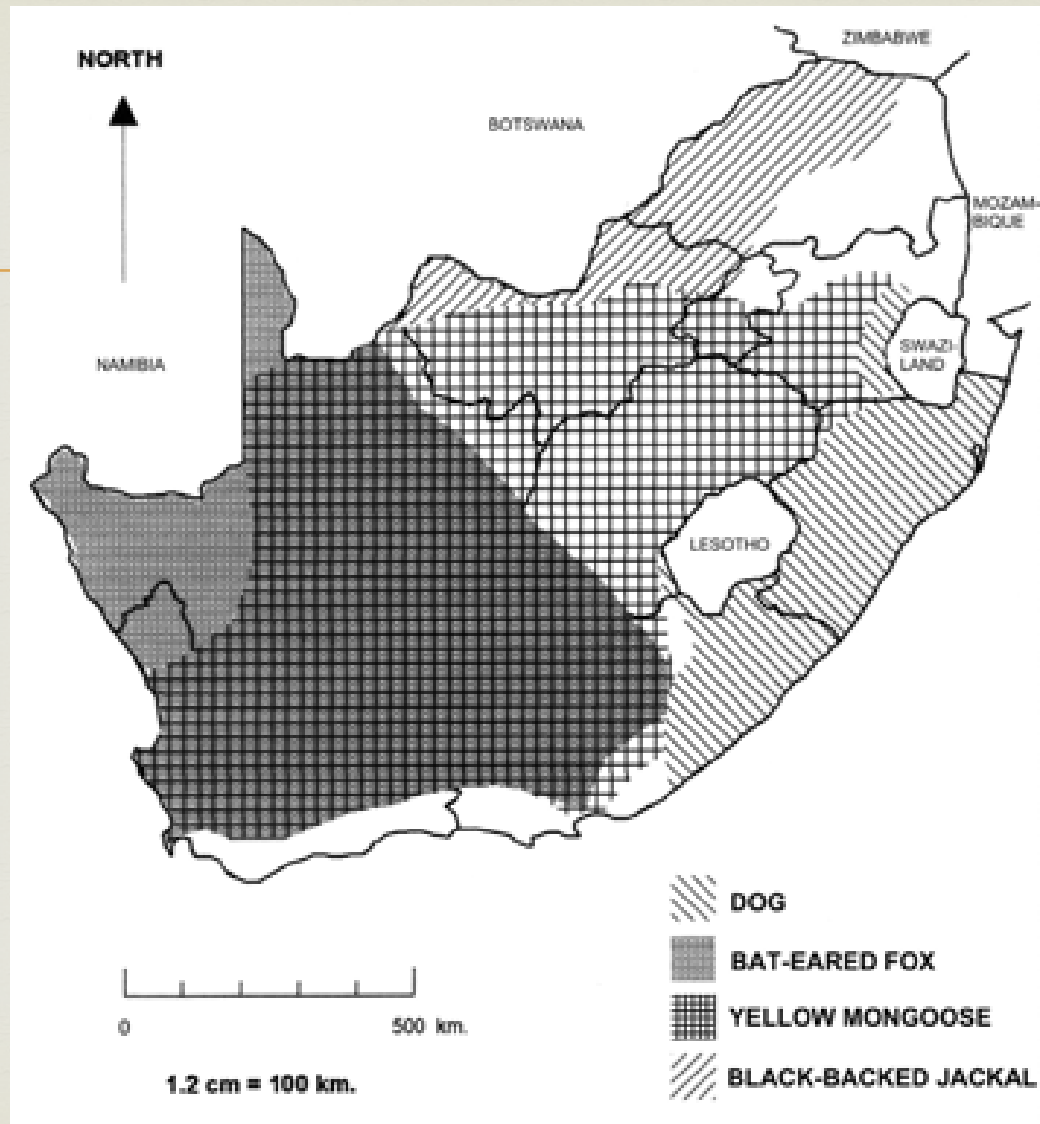




# Africa









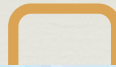
# Rabies Transmission:



- Bites are the **most common route (high titer in saliva)**
- Small abrasions or cuts from animal's teeth –
- Mucous membrane contact with virus – saliva?
  - Including nasal mucosa (bat strains) – **not well-defined**
  - Corneal/tissue transplants from infected donors
    - 3 solid organ recipients in Alabama in 2004 – all died
    - 8 global corneal transplant recipients have died of rabies
  - Laboratory exposure to aerosols or needle sticks (very rare)
  - Abrasions/wounds licked by an infected animal
  - Rabies in saliva a few days before “madness,” lick a cut/wound
- Global: **dogs, dogs, dogs > bats > other mammals (skunk, fox, raccoon)**
  - Peak in summer
  - # global risk group – young males
  - No racial, genetic differences in susceptibility



# Rabies-vectors





# Understand Rabies: Pathogenesis



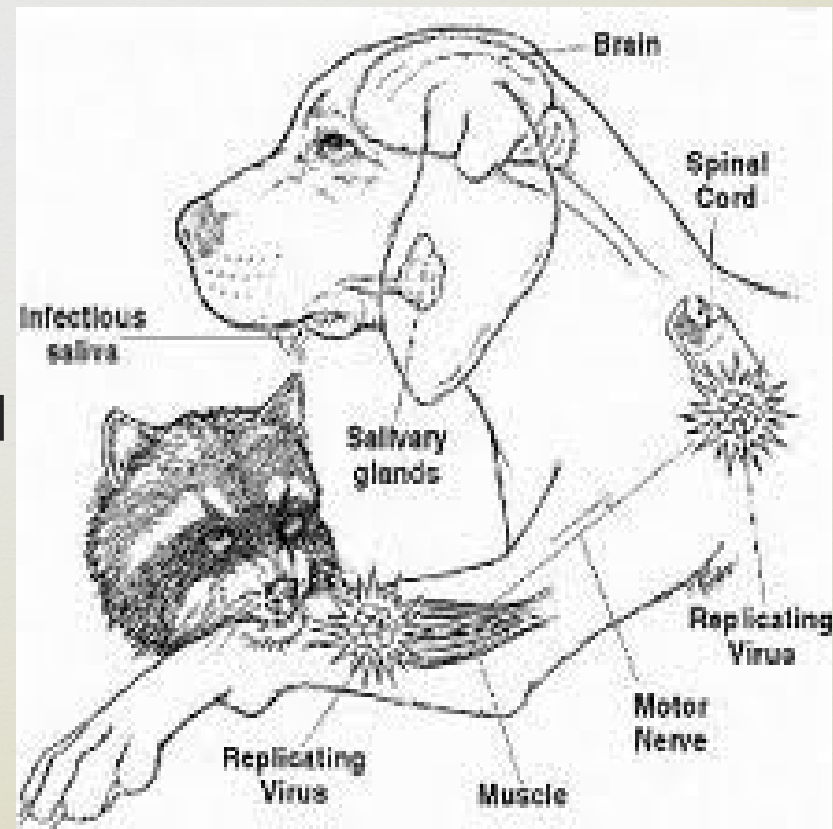
After bite occurs:

- ! virus localized in wound area – replication in myocytes?
- ! latent period: days to years ... then **spread up neurons to CNS**
- ! possibly shortened with stress, steroids, large inoculums, etc

After CNS infection, rapid spread

- ! salivary glands infected shortly after CNS (varies)
- ! Faster in dogs than humans?

Russian Website: [Russia-IC.com](http://Russia-IC.com)  
**LOCAL - NERVE - CNS - SALIVA**





# Understand Rabies: Clinical Features



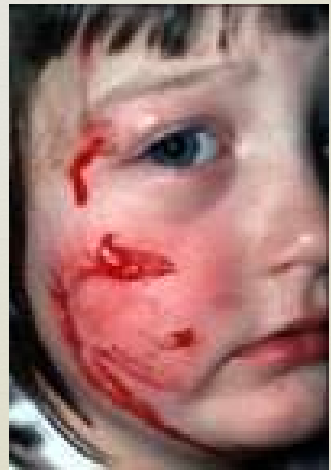
- ▢ Incubation
  - ⚠ Mean: 20 - 60 days, Extremes occur
  - ⚠ **Range : 5-6 days to 19+ years**
- ▢ Prodrome – strange symptoms
- ▢ Acute neurological phase
- ▢ Coma
- ▢ Resolution
  - ⚠ Almost universally: death
  - ⚠ Anecdotally: recovery with prolonged ICU and antiviral drugs (Approx 6-7 people)





# Understand Rabies: Incubation

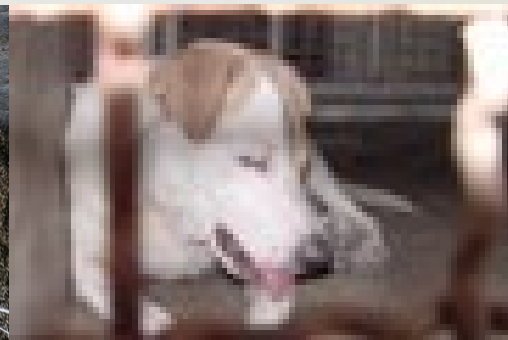
- In humans, typically 1 – 3 months
  - ! 84% within 90 days, **99% < 1 year**
  - ! May be as brief as 4 days
  - ! Cases documented 19 years post-exposure
  - ! Shorter period: little room for delay if ...
    - Bites to face/neck – close to brain via cranial nerves  
(Virus travels up nerves at between 12 and 100 mm/day)
- \*We try to give vaccine and RIG ASAP for head and neck bites!!**
  - Younger patients
  - Multiple bites, high viral dose
- During incubation:
  - ! Clinically silent
  - ! No detectable antibody





# Understand Rabies - Acute Neurologic Phase

- Onset with development of objective CNS signs
  - ❗ Typical duration 2 – 7 days
- Two clinical states
  - ❗ Furious / classical / agitated ~80% (MADNESS)
    - Look for “Odd behavior” – a night animal seen in daytime
  - ❗ Paralytic / dumb ~20%





# Understand Rabies - Serum Diagnosis



- ❑ **No technique** for diagnosis prior to CNS infection
- ❑ Virus **does not stimulate antibody** while *“immunologically protected”* at bite site or ascending up neurons
- ❑ Antibody production begins **after CNS infection** (When the Game is Over):
  - ⚠️ rabies serum neutralizing Ab not detected until 6th day of clinical illness (The **serum** response is **SLOW**)
  - ⚠️ CSF Ab may be negative as long as 7 days after detection of serum Ab (**CSF** response is **VERY SLOW**)
  - ⚠️ if no post exposure prophylaxis, 50% show Ab by day 8 and **100% by day 15 of clinical disease**
  - ⚠️ Steroids, interferon may delay antibody development



# 5 Rules on How To Deal With Rabies:

1. Understand the disease, know your “region”
  - Rabies is very regional, distinct local vectors (animals)
2. Avoid Getting Bit
4. Low threshold for PEP
3. If “Bit”
  - clean the wound aggressively for “PEP” post-exposure prophylaxis
  - Must have excellent information and full control of risk factors to decide to “not” give prophylaxis
5. Follow the rules ASAP
  - most rabies due to delays, or not following the



# Rabies Vaccines: Try to use U.S. lots:

- **Many vaccines available outside the USA**
  - ❗ Some less immunogenic, poorly purified –
  - ❗ Increased association with neurologic and other side effects
- **Two inactivated US vaccines, ~100% efficacious if correctly used**
  - ❗ HDCV- Human Diploid Cell Vaccine
    - Product: Imovax Rabies (HDCV for pre or post-exposure)
    - Manufacturer: Sanofi Pasteur, licensed **1980**
  - ❗ PCECV - Purified Chick Embryo Cell, grown in chicken fibroblasts
    - If hypersensitivity to other vaccines, i.e. frequent boosters
    - Chicken allergy does not preclude use
    - Product: RabAvert (PCECV for pre/post-exp), Manufacturer: Novartis, licensed **1997**
- Standard use = 1.0 cc IM



# Rabies Immune Globulin (HRIG):

- Historically: Used since mid-1950's
  - ⚠ Extensive WHO studies in the Middle East
- All US/Western IG products are very safe!
  - ⚠ HyperRab™; and Imogam®
- Covers the initial 2 weeks for patients to develop their own immunity
- **Not used** if prior immunization
- Simple rules:
  - ⚠ Give once
  - ⚠ Within and including 7 days, ***then no benefit afterwards***
  - ⚠ ***Do not overdose*** (may reduce vaccine efficacy)
    - 20 IU/Kg of body weight
  - ⚠ All or most near the wound if possible, remainder IM deltoid or thigh – **NEVER IV**
  - ⚠ ***Never anatomically close*** to the vaccine site





## Postexposure Prophylaxis for Non-immunized Individuals

| Treatment              | Regimen   |
|------------------------|---|
| <b>Wound cleansing</b> | All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.  |
| <b>RIG</b>             | If possible, the <b>full dose</b> should be infiltrated around any wound(s) and any remaining volume should be administered IM at an anatomical site distant from vaccine administration. Also, RIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be given. |
| <b>Vaccine</b>         | HDCV or PCECV 1.0 mL, IM (deltoid area ), one each on days 0 , 3, 7, and 14.  |

## Postexposure Prophylaxis for Previously Immunized Individuals

| Treatment              | Regimen  |
|------------------------|--|
| <b>Wound cleansing</b> | All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds. |
| <b>RIG</b>             | RIG should <b>not</b> be administered.   |
| <b>Vaccine</b>         | HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 and 3.   |



# 4 sample sites required by CDC to Rule Out rabies (To prove you do NOT have rabies ....)



**1. Saliva for virus:** Collect with dropper and place in sterile container. Tracheal aspirates, sputa not suitable

- RT-PCR
- Virus isolation

**2. Neck biopsy:** 5-6 mm diameter punch from nape

- Minimum 10 hair follicles
- Sufficient depth to include **cutaneous nerves** @ base of follicle
- On sterile gauze moistened with sterile water
- **RT-PCR** and **IF** staining for viral Ag in frozen sections

**3 & 4. Serum and CSF serology:**

- Test for Ab with indirect IF and virus neutralization
- If no vaccine or RIG has been given, the presence of serum rabies Ab makes dx, CSF testing unnecessary
- Ab to RABV in CSF, regardless of immunization hx, suggests rabies infection

**\*Brain biopsy** – old histopathology for “Negri” bodies – very specific, lower sensitivity – Best site is the cerebellum or basal ganglia (post mortem)



## Summary: Management and Treatment of Animal Bites



### **Cultures**

- Gram stain, aerobic, and anaerobic cultures

### **Irrigation**

- Normal saline; copious high-pressure

### **Debridement**

- remove necrotic tissue and any foreign bodies

### **Imaging**

- Plain radiographs to rule out foreign body
- CT/MRI if concern for osteomyelitis

**Wound closure** - not usually indicated



## Management and Treatment of Animal Bites



### **Antimicrobial therapy:**

- Prophylactic antibiotics in selected cases
- Coverage based on patient type and specific animal involved

### **Hospitalization Indications:**

- fever, sepsis, spreading cellulitis, substantial edema or crush injury, loss of function, immunocompromised status, or noncompliance

### **Immunizations:**

- Tetanus booster and/or immune globulin
- ? Rabies vaccine and/or immune globulin



## Empiric oral antibiotic therapy for animal bites

| Antibiotic agents   | Adults                               |
|---|--------------------------------------|
| <b>Agent of choice</b>  |                                      |
| Amoxicillin-clavulanate   | 875/125 mg twice daily               |
| <b>Alternate empiric regimens include:</b>                                    |                                      |
| <b>One of the following agents with activity against <i>P. multocida</i>:</b> |                                      |
| Doxycycline*  | 100 mg twice daily                   |
| TMP-SMX*  | 1 double strength tablet twice daily |
| Penicillin VK   | 500 mg four times daily              |
| Cefuroxime  | 500 mg twice daily                   |
| Moxifloxacin  | 400 mg once daily                    |
| <b>PLUS</b>   |                                      |
| <b>One of the following agents with anaerobic activity:</b>                   |                                      |
| Metronidazole   | 500 mg three times daily             |
| Clindamycin*  | 450 mg three times daily             |

UNCLASSIFIED//FOUO





# QUESTIONS?